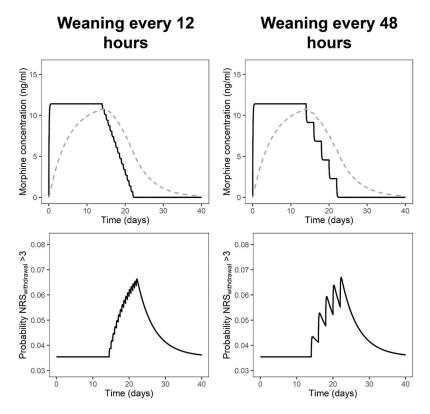
## Towards evidence-based weaning: a mechanism-based pharmacometric model to characterize iatrogenic withdrawal syndrome in critically-ill children

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## Supplemental Material 8: Supplemental Figure S4

## Morphine



**Figure S4.** The impact of time between weaning steps on the risk of iatrogenic withdrawal syndrome (IWS) after 14-day treatment period with continuous intravenous morphine at 20 mcg kg<sup>-1</sup> hr<sup>-1</sup> in a typical patient with a 10 kg body weight. The top row shows the simulated morphine concentrations in plasma (solid black line) and morphine concentrations that the child has become dependent on (dashed grey line). The bottom row shows the predicted probability of an NRS<sub>withdrawal</sub> score above 3, which indicates IWS. In all scenarios, the time between the first reduction in the morphine infusion and the complete discontinuations of the morphine infusion is 8 days.